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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/572,669	01/08/2007	Robert W. Marquis Jr.	PU60511	4597

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SMITHKLINE BEECHAM CORPORATION		
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EXAMINER	
CHANDRAKUMAR, NIZAL S	

ART UNIT	PAPER NUMBER
1625	

NOTIFICATION DATE	DELIVERY MODE
12/11/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

US_cipkop@gsk.com

Office Action Summary

Application No.

10/572,669

Applicant(s)

MARQUIS JR., ROBERT W.

Examiner

Nizal S. Chandrakumar

Art Unit

1625

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-11 is/are pending in the application.
- 4a) Of the above claim(s) 3-11 is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1 is/are rejected.
- 7) ☒ Claim(s) 2 is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. ____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date ____.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. ____.
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: ____.

DETAILED ACTION

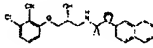
This application file 01/08/2007 is a 371 of PCT/US04/31120 09/23/2004 which claims benefit of 60/506,001 09/24/2003.

Claims 1-11 are pending.

Election/Restrictions

1. During a telephone conversation with Soma G. Simon on 11/28/2007 a provisional election was made with traverse to prosecute the invention of compound claims 1 and 2. Affirmation of this election must be made by applicant in replying to this Office action.

2. The traversal is on the grounds that the claims 3-11 drawn to pharmaceutical methods are related to the compounds of claims 1 and 2. This is not found to be persuasive because the inventions of claim 1-2 and 3-11 are independent and distinct.

Inventions 1-2 and 3-11 are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product. See MPEP § 806.05(h). In the instant case the process of using the product can be practiced with NPS 2143  (see Nemeth et al. Pharmacology and Experimental Therapeutics, 299(1), 323-331, 2001). The compounds in general are not limited to pharmaceutical use.

Further the compounds are classified in class 549/60 and 549/274 while the medicinal aspects are classified in class 514/444.

3. Because these inventions are independent or distinct for the reasons given above and there would be a serious burden on the examiner if restriction is not required because the inventions require a different field of search (see MPEP § 808.02), restriction for examination purposes as indicated is proper.

4. As such the restriction requirement is deemed proper and is therefore made FINAL.

5. Claims 3-11 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

6. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Claim Rejections - 35 USC § 112

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a limited number of compounds of the formula, does not reasonably provide enablement for the plurality of possible structures claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims. With respect to making of the compounds the specification is enabling for variables R1, R2 and R4. The specification is enabling for one possibility for the variable R3. It is not seen, for example, where in the specification, enablement is present for R3 being other than C4 alkylene. With respect to use of the compounds, the specification does not disclose pharmacological properties for any of the claimed compounds.

Enablement is considered in view of the Wands factors (MPEP 2164.01 (a)). These include: (1) breadth of the claims; (2) nature of the invention; (3) state of the prior art; (4) amount of direction provided by the inventor; (5) the level of predictability in the art; (6) the existence of working examples; (7) quantity of experimentation needed to make or use the invention based on the content of the disclosure; and (8)

relative skill in the art.

All of the factors have been considered with regard to the claims, with the most relevant factors discussed below:

The claims are drawn to metacyclophane compounds in which the ring size varies from 11 to 15 with optionally substituted various alkylene and alkenyl possibilities for the ring chains making the number of conceivable structures large.

The level of skill in the art is high. However, due to the unpredictability in the art of organic and medicinal chemistry, it is noted that each embodiment of the invention is required to be individually assessed for viability.

With respect to the crucial ring forming reaction, the direction provided in the specification is limited to one R3 variable. This lone example relates to the macro-esterification of a hydroxy acid wherein the R3 ring chain is C4-alkylene group. The preparation of such cyclization precursors wherein the R3 could be varied, is known to one skilled in the art. However the feasibility of large ring cyclization depends not only on the reaction conditions, for example to force unimolecular reactions, but also on the conformational aspect of the substrate for cyclization. The 15% yield obtained in this lone example at high-dilution condition is reflective of the difficulty and unpredictability in achieving the geometry (transition state) necessary for the formation of cyclophanes and macrocyclic compounds. For example, it is highly questionable if an unsaturated trans alkene compound such as the one of Example 2c would be susceptible to cyclization under any condition. The specification does not provide citations (commercial or literature) for procuring the starting materials usable that could substitute for the lack of working examples with respect to non-enabled R3 variables.

In spite of major advances in strategies such as olefin metathesis, the state of the art of organic synthesis is unpredictable with respect to making cyclophanes and macrocyclic compounds. For example, the geometry required for the formation of rings limits what kind (saturated or unsaturated) of R3 chains or substituents on R3 can be present in the cyclization precursor. The existence of such unpredictabilities and uncertainties would prevent one of ordinary skill in the art from accepting any process such as the one presented in the lone working example on its face as universally applicable for all the substitutions for R3 claimed.

The quantity of experimentation: For the reasons presented above, in order to utilize the invention as claimed, that is to make and use the claimed compounds, the skilled artisan would be presented with an unpredictable amount of experimentation. The instant disclosure is broad and generic. Further, based on the lack of disclosure with respect to the biological activity of the compounds of the formula (I), it is not clear what specific embodiments would be required in order for one of ordinary skill in the art at the time the invention was made to practice the instant invention commensurate in scope of the claims.

Limiting R3 to C3-C5 alkylene would overcome the above rejection.

The specific compounds of claim 2 are free of prior art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nizal S. Chandrakumar whose telephone number is 571-272-6202. The examiner can normally be reached on 8.30 am - 5 pm Monday- Friday.


If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached at 571-272-0867 or Primary Examiner D. Margaret Seaman can be reached at 571-272-0694. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Application/Control Number:
10/572,669
Art Unit: 1625

Page 6

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.


Nizal S. Chandrakumar


D. MARGARET SEAMAN
PRIMARY EXAMINER